Parkinsonism and Related Disorders 132 (2025) 107263

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Vibro-tactile stimulation of the neck induces head righting in people with cervical dystonia

Laura Avanzino [a,b,*,1], Jiapeng Xu [c,1], Davide Martino [d], Antonella Conte [e,f], Stephanie Standal [g], Parisa Salehi [g], Sara Terranova [a], Gaia Bonassi [b,h], Parisa Alizadeh [d], Janet Adesewa Adeoti [d], Daniele Belvisi [e,f], Matteo Costanzo [f,i], Jinseok Oh [c], Jürgen Konczak [c,j]

[a] Department of Experimental Medicine at the University of Genoa, Italy
[b] IRCCS Policlinico San Martino, Genoa, Italy
[c] Human Sensorimotor Control Laboratory, School of Kinesiology, University of Minnesota, USA
[d] Department of Clinical Neurosciences, University of Calgary, Canada
[e] IRCCS Neuromed, Pozzilli, IS, Italy
[f] Department of Human Neurosciences, Sapienza University of Rome, Italy
[g] Department of Rehabilitation Medicine, Physical Medicine & Rehabilitation Division, University of Minnesota, USA
[h] Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genoa, Genoa, Italy
[i] Department of Neuroscience, Istituto Superiore di Sanità, Rome, Italy
[j] Center for Clinical Movement Science, University of Minnesota, USA

ARTICLE INFO

Keywords:
Human
Movement disorder
Proprioception
Somatosensory
Vibration

ABSTRACT

Introduction: Cervical dystonia (CD) is characterized by involuntary neck muscle spasms that lead to abnormal head movements or postures. It is associated with somatosensory (tactile and proprioceptive) dysfunction. Here we tested whether vibro-tactile stimulation (VTS) of the cervical muscles constitutes a non-invasive form of neuromodulation of the somatosensory system that can provide temporary symptom relief for people with CD.
Material and method: In a multi-centre study, 67 CD patients (44 female) received VTS to sternocleidomastoid and/or trapezius muscles for up to 45 min under 9 different stimulation conditions. Retention was assessed 1, 5 and 20 min past VTS. Head angles and neck muscle EMG were recorded. The primary outcome measure was a head angle index (HAI), a composite measure reflecting the head deviation across the three axes of the head.
Results: After identifying the most effective VTS condition for each participant, analysis showed that 85 % (57/67) of participants experienced an improvement in HAI of at least 10 % during the application of VTS. HAI improved by 50 % or higher in 26/67 of participants. For those responding to VTS, the effects tended to decay within 20 min. For the different CD phenotypes several stimulation sites could induce similarly large relative improvements in head posture.
Conclusion: The study provides first systematic evidence that cervical VTS can induce fast-acting improvements in abnormal head posture in patients with CD. It demonstrates that a stimulation of somatosensory afferent networks modulates the innervation of dystonic muscles. It highlights the potential of cervical VTS as an adjuvant, non-invasive neuromodulation treatment in CD.

Abbreviations: CI, confidence interval; CD, cervical dystonia; BoNT, Botulinum neurotoxin; FD, focal dystonia; HAI, head angle index; MAA, mean absolute angle; ROM, anatomical range of motion; SCM, sternocleidomastoid muscle; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale; TRP, trapezius muscle; VTS, vibro-tactile stimulation.

* Corresponding author. Department of Experiment Medicine, section of Human Physiology University of Genova, Viale Benedetto XV/3, Genoa, Italy.
E-mail address: lavanzino76@gmail.com (L. Avanzino).

[1] Xu and Avanzino contributed equally to this manuscript.

https://doi.org/10.1016/j.parkreldis.2025.107263
Received 10 October 2024; Received in revised form 27 December 2024; Accepted 4 January 2025
Available online 16 January 2025

1. Introduction

Cervical dystonia (CD) is a form of focal dystonia (FD) characterized by involuntary contractions of neck muscles that lead to intermittent or sustained abnormal head movements and posture that are often associated with pain [1]. Current treatment options for CD are limited and mainly consist of Botulinum neurotoxin (BoNT) injections in the dystonic muscles or invasive deep brain stimulation (DBS) [2,3]. The exact pathomechanism of CD and other types of FD is unknown. Empirical reports on the loss of inhibition at cortical [4,5], brainstem [6] and spinal [7] levels, altered synaptic plasticity [8,9] and altered functional connectivity between cortical-subcortical sensorimotor areas [10], all indicate that FD is a network disorder. Moreover, there is consistent clinical and neurophysiological evidence indicating that abnormal processing of tactile, proprioceptive, and nociceptive afferents is part of the pathophysiology (for review see Ref. [11]) resulting in reduced proprioceptive acuity of both dystonic and non-dystonic body segments in FD [12–15]. Underlying neuroanatomical and neurophysiological abnormalities of this observed proprioceptive-motor deficit are undifferentiated or "smeared" finger representations in somatosensory and motor cortex in people with writer's cramp [16–18] and an excessive rise of premotor/motor cortical beta-oscillations over somatosensory-motor cortical areas during motor preparation in CD [19].

These observations open an avenue to explore the usefulness of vibro-tactile stimulation (VTS) as a non-invasive method to modulate somatosensory-motor networks with the aim of alleviating dystonic symptoms in focal dystonia. VTS stimulates proprioceptive mechanoreceptors such as muscle spindles [20–22] and cutaneous mechanoreceptors affecting both motor behaviour and proprioception [23–25]. VTS induces fast and consistent central responses. It alters regional cerebral blood flow of contralateral sensorimotor cortex in patients with blepharospasm and writer's cramp [26,27]. It reduces the excessive levels of neuronal synchronization over sensorimotor cortex in people with laryngeal dystonia [28], an electrocortical response similar to the response observed in patients with CD who apply effective sensory tricks [29]. Moreover, VTS modulates neural responses in subcortical structures as neck muscle vibration instantaneously alters pallidal neuron activity and modulates pallido-cerebellar connectivity in people with CD [30]. Thus, proprioceptive-tactile afferent signals from mechanoreceptors embedded in the skin and muscles significantly influence a central network comprising cerebellum, basal ganglia, thalamus, and somatosensory-motor cortical areas.

There is initial evidence that VTS can reduce symptoms in focal dystonia. A case study reported that VTS applied to trapezius muscles normalized the head posture of a patient with torticollis [31]. Our recent work demonstrated that 69 % of patients with laryngeal dystonia exhibited a reduction of their voice symptoms during VTS, which persisted for 20 min past VTS [28]. However, no studies have systematically examined the magnitude of the effect of VTS on head posture, delineated the response rate in a larger sample of CD participants and documented how the various CD phenotypes respond to stimulating specific muscle groups. To close this knowledge gap, this multi-centre clinical trial assessed the effect of a single session of neck muscle VTS in a large cohort of 67 patients with CD, recording kinematic data of head position and the associated electromyography of the affected neck muscles.

2. Material and methods

2.1. Participants

A total of 67 participants with CD (44 female; mean age ± SD: 61.1 ± 12.5 years) were recruited from four centres. Exclusion criteria were: 1) presence of other neurological disorders, 2) Mini Mental State Examination score <24, 3) presence of sensory abnormalities not associated with CD, and 4) cognitive deficits that impair understanding of instructions and participation. We adopted the *Toronto Western Spasmodic Torticollis Rating Scale* (TWSTRS) to assess the severity (range, 0–35), disability (0–30), and pain (0–20) of CD symptoms prior to testing. Table 1 summarizes the key clinical characteristics of the sample (for individual demographic and clinical characteristics, see Table S1, Supplementary Materials). Participants receiving BoNT injections were seen within two weeks before or one week after a BoNT injection. The experimental protocol was approved by each centre's ethics committee. Consent from all participants was obtained prior to testing.

2.2. Experimental devices and data acquisition

2.2.1. Vibro-tactile stimulation

For VTS, four lightweight, encapsulated vibration motors (Model 307–100, Pico Vibe, Precision Microdrives Ltd., London, UK; diameter: 8.8. mm, length 25 mm) were placed in tandem over the skin above the sternocleidomastoid (SCM) and trapezius (TRP) muscles (see Fig. 1A) as the most frequently affected muscles in CD [32]. At 1.2V DC, the vibration frequency was approximately 100 Hz with a vibration amplitude of 1.7G. Stimulation parameters were selected based on previous studies demonstrating that a vibration frequency of 100 Hz modulates neuronal synchronization over sensorimotor cortex in patients with laryngeal dystonia [28] and induces kinaesthetic illusions in humans by acting on muscle spindle [20,21,33,34].

2.2.2. Electromyography

Surface electromyography of SCM and TRP muscles was recorded at a 2 kHz sampling frequency. For SCM, the electrodes were attached at 2/3 of the distance between the sternal notch and the mastoid process. For TRP, the electrodes were attached at 1/2 of the distance between acromion to the C7 vertebra (see Fig. 1A).

2.2.3. Kinematic data acquisition

A wireless inclinometer (BWT901CL, WitMotion Shenzhen Co. Ltd., China) was attached to the participant's forehead to record kinematic data of head position at a sampling frequency of 200Hz**.** Coordinate axes of the inclinometer were aligned to the anatomical axes of a participant's head.

2.3. Experimental design and procedure

The study applied a single session, single group experimental design. The independent variable was the VTS stimulation condition. Each participant received VTS in up to nine conditions that can be classified into four different categories (see Fig. 1B): *single muscle stimulation*

Table 1
Summary of clinical characteristics of all study participants across the four sites. CD manifestations were examined by trained movement disorder specialists when the patient visited the clinic prior to testing. Total sample size was n = 67. Note that most participants presented with complex symptom patterns, i.e., a combination of phenotypes.

Demographic and clinical feature	
Sex	23M/44F
Age (Mean ± SD)	61.1 ± 12.5 yrs.
Disease duration (Mean ± SD)	13.9 ± 12.7 yrs.
TWTSRS severity subscale (Mean ± SD) (0 = none; max. = 35)	16.1 ± 6.2
TWTSRS disability subscale (Mean ± SD) (0 = none; max. = 30)	10.4 ± 5.9
TWTSRS pain subscale (Mean ± SD) (0 = none; max. = 20)	6.4 ± 5.6
Receiving botulinum toxin type A treatment	60/67 (90 %)
Interval between injection sessions (Mean ± SD)	12.6 ± 2.3 weeks
Symptom presentation	
Complex symptom pattern of CD	58/67 (87 %)
Torticollis	63/67 (94 %)
Laterocollis	53/67 (79 %)
Anterocollis	20/67 (30 %)
Retrocollis	13/67 (19 %)

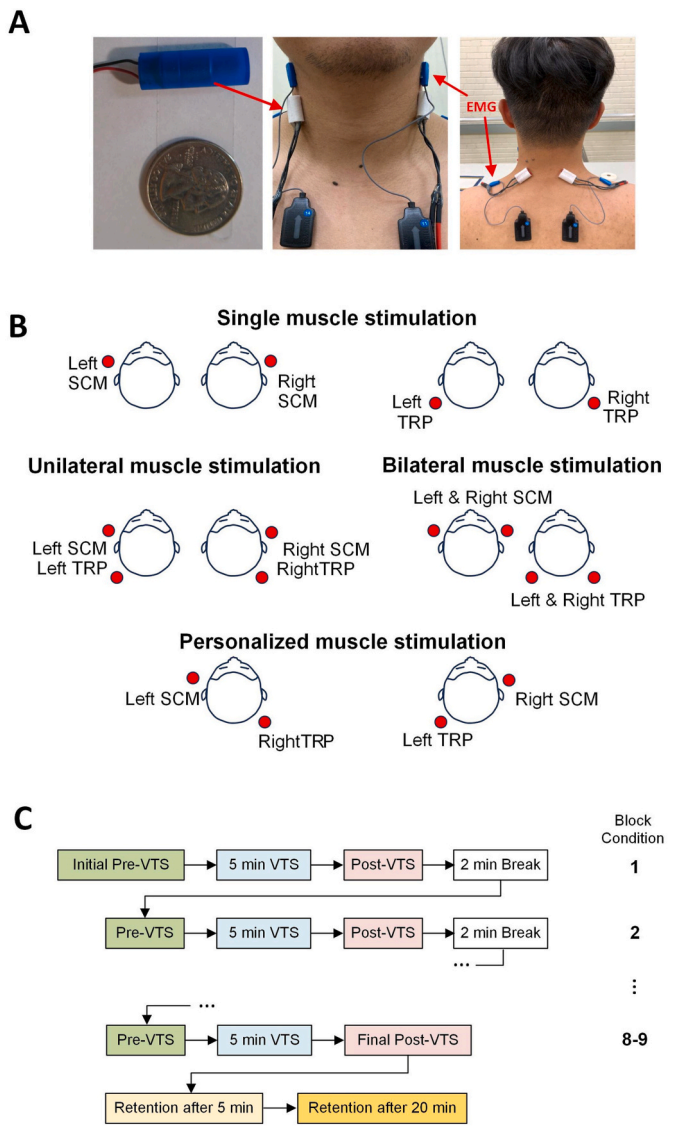

Fig. 1. Experimental device, stimulation conditions and experiment protocol. A. Image of encapsulated vibrator (left figure) and vibrator/sEMG electrodes placement (middle and right figures) at the sternocleidomastoid and upper trapezius muscles. **B.** Graphic of the various sites and conditions for applying vibro-tactile stimulation. **C.** Process diagram of the experimental protocol. Each block corresponds to one of the conditions illustrated in panel B. The order of conditions was randomized across participants.

(stimulating right SCM, left SCM, right TRP, or left TRP individually), *unilateral muscle stimulation* (stimulating left SCM and TRP or right SCM and TRP at the same time), *bilateral muscle stimulation* (stimulating left and right SCM or left and right TRP at the same time), and a *personalized muscle stimulation* (focusing on those SCM and TRP muscles that received BoNT injections). The order of presentation of conditions was randomized across all participants.

Once the participants arrived at the centre, a clinical evaluation of CD was performed using the TWSTRS. During the subsequent recording, participants sat comfortably in a chair, and kept the upper body in an upright stationary position with eyes open. They were asked not to resist the involuntary muscle contraction and to let their neck assume the dystonic posture once it was symptomatic. Testing started with a 2-min baseline assessment data collection prior to attaching the vibrators to the SCM and TRP muscle. Within each stimulation condition, the participant completed a 2-min pre-stimulation assessment data collection (pre-VTS), a 5-min data collection with continuous VTS (VTS-ON), and a 2-min post-stimulation assessment (post-VTS). Between stimulation conditions, there was a 2-min break. Retention assessments were performed 5 (RET5) and 20 min (RET20) after the last VTS treatment block (see Fig. 1C).

2.4. Kinematic and EMG time-series data processing

For the baseline, pre-VTS and retention data series, the first minute, and for the 5-min VTS-ON data sets, the fifth minute segments of the continuous raw kinematic and EMG time-series data were truncated and used for analysis. For the 2-min post-VTS datasets, only the first minute was used because this period reflected the immediate effect after cessation of VTS.

The kinematic data were low-pass filtered at 10 Hz to eliminate the high-frequency components in head angle data (dystonic movement frequency is between 0.1 and 9 Hz [35]). Then, respective head angles around the three anatomical reference axes of head relative to the upright, neutral head position were derived (yaw: longitudinal axis; roll: anterior-posterior axis; pitch: medio-lateral axis) [36,37]. For each angle time-series segment, the *mean absolute angle* (MAA) was calculated. Previous research on healthy individuals had established the boundaries for maximum angular displacement of the head when keeping the head in an upright neutral position [36]. We used these values as thresholds to determine a specific CD manifestation (torticollis: yaw angle: >4.2°; laterocollis: roll angle >2.3°; antero/retrocollis: pitch >7.2°).

For the EMG data, the DC offset of each channel was removed by calculating and subtracting its respective mean. A 100Hz low-pass filter and appropriate notch filters were applied to eliminate high-frequency components and electrical line noise (bandstop frequency: 55Hz–65Hz for 60 Hz AC in US/Canada and 45Hz–55Hz for 50 Hz AC in Italy).

2.5. Outcome measures

To capture complex head posture abnormalities across the several head axes in a single, objective outcome measure, we derived a head angle index (HAI) based on the MAA values and the known anatomical range of motion (ROM) across each head axis. The respective formula is:

$$HAI = \frac{MAA_{yaw}}{ROM_{yaw}} + \frac{MAA_{roll}}{ROM_{roll}} + \frac{MAA_{pitch}}{ROM_{pitch}} \quad (unitless) \tag{1}$$

ROM for each axis refers to the known anthropometric values of healthy adults (yaw = 90°, roll = 45°, pitch = 80° [38,39]. HAI values can range between 0 and 3. A value of 0 indicates perfectly upright head position. Values between 0.5 and 1 indicate a moderate to severe head posture abnormality around one axis (e.g., 45–90° to the left for someone with left torticollis). To quantify levels of muscle contraction over time, the root-mean-square was extracted for each pre-processed EMG channel using:

$$EMG_{RMS} = \sqrt{\frac{1}{N}\sum_{n=1}^{N} |X_n|^2} \tag{2}$$

where Xn is the nth data point of time-series EMG. N was 120000 (2000 Hz × 60 s) for each 1-min data segment.

2.6. Data analysis

The relative change with respect to pre-VTS in HAI was calculated for two time points (VTS-ON, post-VTS). The relative change in EMG_{RMS} was only calculated for post-VTS (EMG signals were contaminated by the vibration during VTS-ON). Relative change was calculated as follows:

$$rHAI \text{ or } rEMG_{RMS} = \frac{Timepoint - pre\_VTS}{pre\_VTS} \times 100 \quad (\%) \tag{3}$$

A negative value in rHAI reflected an improved, more upright head

posture, a negative value in $rEMG_{RMS}$ indicated a reduction in the overall muscle activity.

For each participant, stimulation conditions that resulted in more than 10 % relative improvement in HAI at VTS-ON vs. pre-VTS were identified. The mean relative HAI improvement across participants and the response rate were summarized for each stimulation condition within each CD phenotype group (torticollis, laterocollis, anterocollis, and retrocollis). The response rate of a particular stimulation condition was defined as the ratio between the number of participants who showed 10 % or higher HAI improvement and the total number of participants within a CD phenotype group. The optimal muscle stimulation profile for each CD manifestation was identified as the stimulation condition that resulted in the largest mean relative improvement in HAI.

2.7. Statistical analysis

Results of respective Shapiro-Wilk tests indicated that the absolute and relative HAI and EMG_{RMS} data did not follow a normal distribution. Consequently, non-parametric statistics were applied. Wilcoxon signed-rank tests were performed to compare the HAI at pre-VTS, VTS-ON, and post-VTS for the stimulation condition that yielded the largest relative reduction in HAI (most effective stimulation). The HAI obtained at the initial pre-VTS, the post-VTS of the final treatment block (final post-VTS) and the retention time points (RET5 and RET20, see Fig. 1C) were compared to investigate the retention effect. To account for multiple comparisons, p-values were adjusted using the Benjamini-Hochberg method [40] and denoted as p_{adj}. The initial significance level was set to $p = 0.05$. A stepwise linear regression model analysis (stepAIC function, MASS package in R, version 7.3–58.1) was performed to determine predictors of the relative change in HAI (for details, see Supplementary Materials).

3. Results

HAI at initial pre-VTS time point was moderately and positively correlated with the severity sub-scale of the TWSTRS ($r = 0.37$, $p < 0.01$), indicating good convergent validity of the index. The relevant descriptive statistics for initial HAI values prior to VTS application are detailed in Table 2. The HAI values at the initial pre-VTS time point reflect a participant's baseline level of head deviation before the application of VTS. The application of VTS proved to be safe. No participant reported an adverse event.

3.1. Effects of VTS on head posture

Fig. 2A shows exemplar time-series head angle data for two

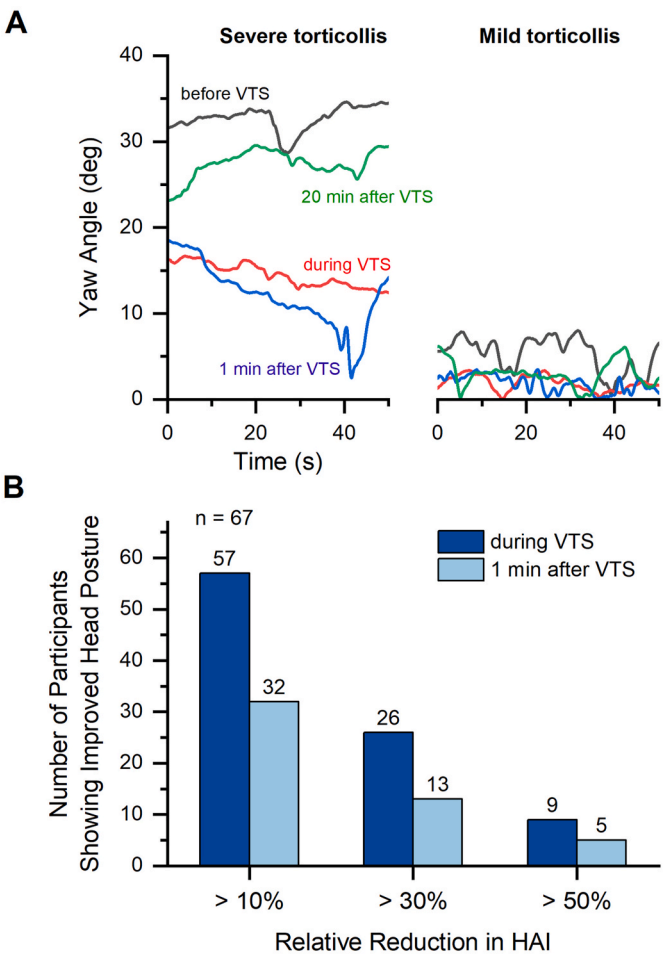

Fig. 2. Changes in head posture due to cervical VTS. A. Exemplar time series data of the yaw head angle (rotation to the left or right) in two patients with torticollis. Note that the large and fast change in head angle in the more severely affected participant. The effect decayed slowly but was still visible 20 min past VTS. The more mildly affected participant also showed an effect but given the smaller deviation from the neutral head position, the magnitude of head angle change was smaller. An angle of 0° indicates a straight-ahead position. **B.** Magnitude and frequency of improvement in abnormal head posture due to VTS. Shown is the relative change in HAI during VTS-ON and post-VTS relative to the pre-VTS baseline for each participant at the most effective stimulation condition.

Table 2
The table reports (i) HAI median values at baseline prior to VTS application (i.e., Baseline) and (ii) absolute changes in HAI during VTS (VTS ON- Baseline) and (iii) 1 min after the cessation of VTS (Post-VTS - Baseline). A participant's CD phenotype was determined based on the recorded head angles. Participants who presented with complex CD manifestations pattern were assigned to more than one CD phenotype group. Theoretically, baseline HAI values can range between 0 and 3. However, note that a value of 1 already indicates a severely compromised head posture around one or two head axes, with a head at or near its maximum range of motion. Absolute change values (VTS ON- Baseline and Post-VTS – Baseline) represent the median change and the minima and maxima of observed absolute change relative to baseline (initial pre-VTS condition). Negative values indicate a reduction of abnormal head posture.

	Baseline		VTS On – Baseline		Post-VTS - Baseline		N
	Median	Min, Max	Median	Min, Max	Median	Min, Max	
Left torticollis	0.49	(0.10, 1.21)	−0.20	(-0.39, 0.27)	−0.12	(-0.38, 0.40)	14
Right torticollis	0.52	(0.15, 1.18)	−0.08	(-0.63, 0.78)	−0.04	(-0.60, 0.85)	28
Left laterocollis	0.44	(0.08, 1.21)	−0.07	(-0.63, 0.27)	−0.04	(-0.60, 0.40)	24
Right laterocollis	0.42	(0.06, 0.92)	−0.07	(-0.44, 0.78)	0.02	(-0.45, 0.85)	23
Anterocollis	0.65	(0.23, 1.02)	−0.05	(-0.33, 0.78)	−0.03	(-0.31, 0.85)	12
Retrocollis	0.68	(0.14, 1.21)	−0.22	(-0.47, 0.03)	−0.11	(-0.45, 0.03)	12

participants presenting with torticollis. As can be seen, VTS induced a fast and substantial change in head posture in the severely affected participant (Fig. 2A, left panel). An analysis focusing on the condition that induced the largest change in HAI showed that 57/67 (85 %) of participants responded to VTS with a 10 % or higher reduction in HAI (Fig. 2B). HAI was reduced by 50 % or higher in 39 % (26/67) of participants. Those (10/67) showing less than 10 % improvement in HAI presented with mild symptoms. The related paired-comparison analysis indicated that median HAI during and immediately after VTS were significantly smaller than pre-VTS for a participant's most effective stimulation condition (VTS-ON vs. pre-VTS median difference: −0.07 [Q1, Q3: −0.13, −0.03], $Z = -6.28$, $p_{adj} < 0.01$; post-VTS vs. pre-VTS median difference: −0.03 [Q1, Q3: −0.10, 0.00], $Z = -3.99$, $p_{adj} < 0.01$; Fig. 3A).

Collapsing the three angular data sets and considering each participant's values across these three axes yielded a median change in head angle of −4.5° and a maximum change of −47.6° (Fig. 3B). Importantly, CD participants of all phenotypes responded to VTS as shown in Fig. 3C.

To characterize the effect of VTS for the different CD phenotypes, the mean relative improvement in HAI (Fig. 4A) and the corresponding

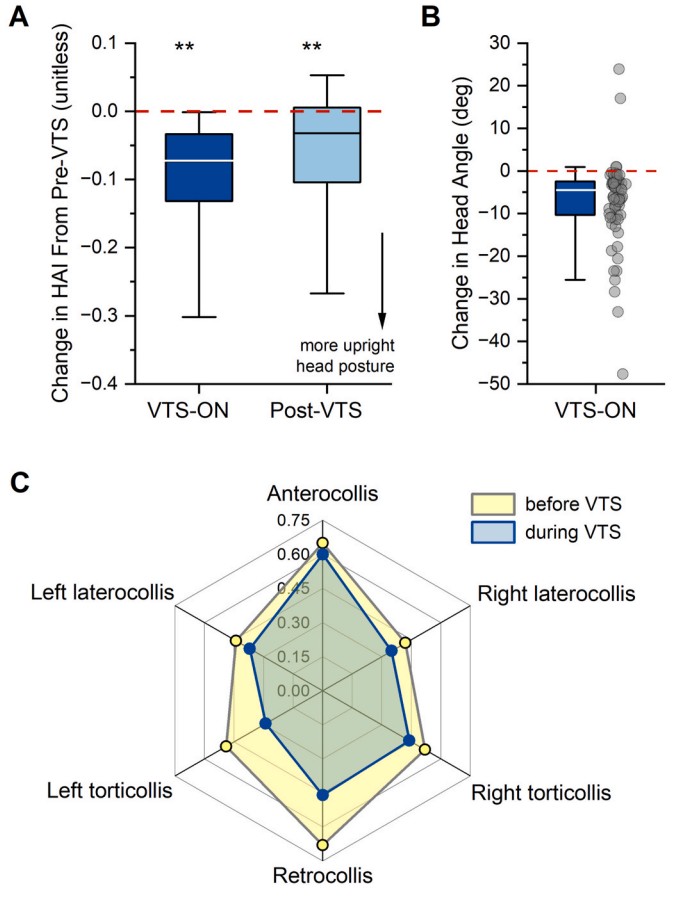

Fig. 3. Changes in HAI and head angle for the most effective individual stimulation condition. A. Median change in HAI during VTS-ON and 1-min post-VTS relative to pre-VTS. HAI reflects 3D head position. For CD symptoms that primarily present with abnormal head angles around one head axis, a value of 0.5–1 indicates a moderate to severe head position abnormality. Negative values indicate improvement towards an upright head posture. The lower and upper whiskers represent the 5th and 95th percentile. Solid lines in each box indicate the median. ** indicates a p-value <0.01 for comparisons relative to pre-VTS. **B.** Changes in head angle during the application of the most effective stimulation condition across all three axes. Negative values indicate the improvement in abnormal head posture. **C.** Radar plot showing the median HAI values for each CD phenotype before and during the application of VTS at the most effective stimulation condition.

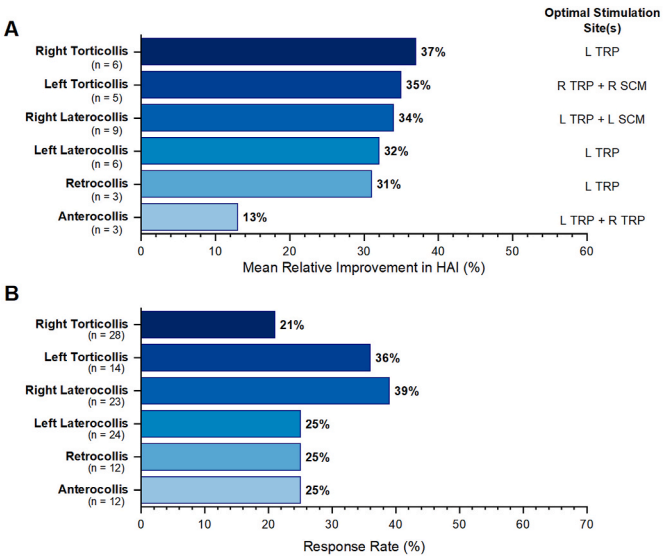

Fig. 4. VTS-induced reduction in HAI and response rate by CD phenotype. A. Mean relative improvement across participants for their optimal muscle stimulation condition for each of the six CD manifestations. The related optimal stimulation site/condition yielding the largest mean relative HAI reduction is indicated. Here, n indicates the number of participants who showed 10 % or higher relative improvement in HAI for such stimulation condition. **B.** Shown is the corresponding response rate for each optimal muscle stimulation condition shown in A. Here, n indicates the number of participants for a CD phenotype subgroup.

response rates for each CD phenotype were determined (Fig. 4B). The personalized stimulation condition, which focused on stimulating the clinically identified dystonic muscles, was not necessarily the optimal stimulation condition. It induced a 12–28 % mean relative improvement in HAI, which was smaller when compared to the muscle stimulation condition that yielded the largest improvement for a specific CD phenotype, respectively (Fig. 4A). To understand the magnitude of the observed VTS effect, the respective median and maximum absolute change in HAI for each CD phenotype is presented in Table 2.

To determine possible VTS effects after the cessation of VTS, we compared the change in HAI at the final post-VTS and the two retention time points of 5 and 20 min (RET5, RET20) relative to the initial pre-VTS time point. Changes in HAI were not significantly different from the initial pre-VTS (final post-VTS vs initial pre-VTS: $Z = -1.78$, $p_{adj} = 0.22$; RET5 vs initial pre-VTS: $Z = -1.40$, $p_{adj} = 0.24$; RET20 vs initial pre-VTS: $Z = -1.11$, $p_{adj} = 0.26$). However, there were 10 participants exhibiting a 10 % or higher relative improvement in HAI at all three time points after VTS treatment session.

Linear regression analysis revealed that neither demographic nor clinical variables were good predictors of VTS effects on head position (for details, see Supplementary Materials). Noteworthy, participants presenting with tremor showed an 11 % greater relative improvement in HAI than the participants who did not present with tremor after controlling for gender (95 % *CI*: 1 to +22 %, $p = 0.04$). A participant's use of a sensory trick was not a clear differentiator between effective vs. ineffective VTS with 44/57 of responders and 6/10 of non-responders using a sensory trick.

3.2. *Electrophysiological and muscle-specific responses to VTS*

The EMG data of 66 participants were recorded and analysed (data of one participant were lost due to a device issue). Dystonic muscle activity was observed in one or more muscles. A total of 30 participants revealed dystonic activity in left SCM, 32 in right SCM, 27 in the left TRP, and 25 in the right TRP. To illustrate the effect of VTS on dystonic muscle

activity, Fig. 5A shows exemplar EMG time-series data before and immediately after the application of the VTS for two different participants. For the more affected participant presenting with left torticollis, right SCM activity decreased by 62 % as the yaw angle was reduced by 19° due to the VTS under the most effective stimulation condition (R TRP + R SCM). For the less affected participant, the left dystonic SCM muscle did not show obvious change in EMG activity although the yaw angle was reduced 4° for the most effective stimulation (L TRP + L SCM).

A systematic analysis of how the various muscle stimulation conditions affected head posture, revealed that for each phenotype several stimulation conditions could be effective. VTS of muscles opposite to the symptoms tended to yield greater change in HAI for participants presenting with torticollis (e.g., right SCM or TRP for left torticollis), while for right laterocollis conditions involving stimulation of left or right SCM induced the largest improvement in head posture (see Fig. 5B).

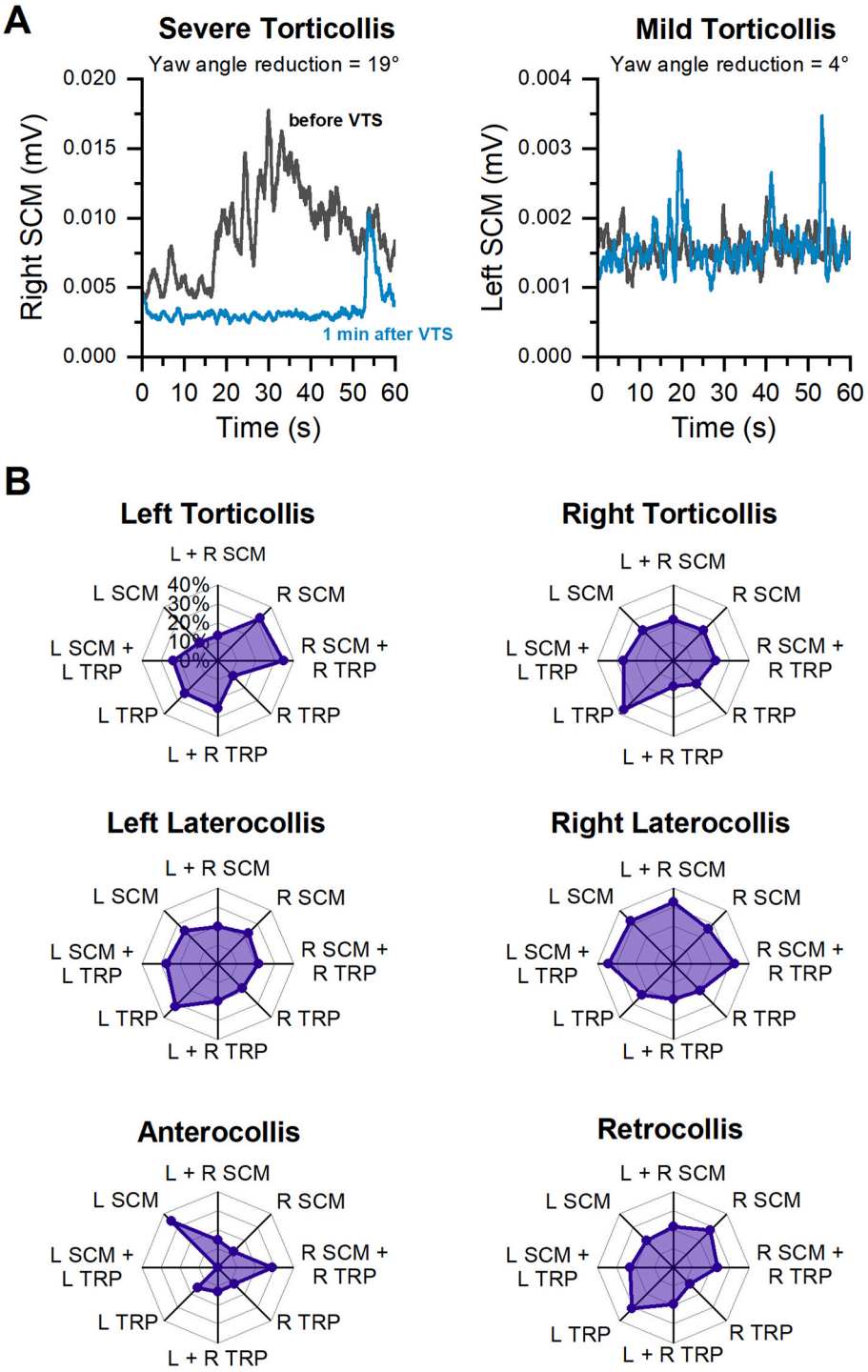

Fig. 5. Muscle-specific responses to VTS. A. Exemplar time-series data of SCM muscle activity of two participants presenting with left and right torticollis before and immediately after the application of VTS. Note that the respective angle time-series data for each participant are shown on Fig. 2A. **B.** Radar plot of muscle response profiles for each CD phenotype. Shown is the mean relative improvement in HAI across participants for each muscle stimulation condition.

4. Discussion

This is the first study to systematically investigate the effect of VTS on head posture in a large sample of people with CD. The main findings are as follows: First, 85 % of participants responded to VTS with 39 % of all participants showing a reduction of HAI of 50 % or higher in at least one stimulation condition. Electromyographic recordings documented that such improvements in head posture were associated with a reduction of dystonic muscle activity. Second, the VTS induced effects in normalizing abnormal head posture decayed fast within 5–20 min. Third, for the various CD phenotypes, several stimulation conditions could induce similarly large relative improvements. Fourth, demographic and clinical measures of disease severity did not predict the rate of observed improvement in head posture. Fifth, the application of VTS was safe. No adverse events were reported.

4.1. Magnitude and duration of VTS effects on head posture in CD

Most CD participants showed mild or moderate symptoms at baseline with relatively small deviations of head position (see Table 1 and Table 2). The mean relative reduction in HAI due to VTS ranged between 13 and 37 % per CD phenotype (see Fig. 3A), with half the participants experiencing a 2.5°–10° reduction in head angles during the application of VTS (see Fig. 3B). We observed larger amplitude changes in the more affected CD participants. For example, for one participant presenting with left torticollis, the total reduction of head angle was 48° during the most effective stimulation (see Fig. 2A) which was associated with a substantial suppression of dystonic SCM muscle activity (see Fig. 5A), demonstrating the potential of neck muscle VTS in normalizing abnormal head posture in more severely affected people with CD.

The observed effects of neck muscle VTS were fast acting within minutes, but also tended to decay quickly after VTS was turned off. At the at 5- and 20-min retention time points the effect on HAI was no longer significant at the group level. There are neurophysiological data suggesting that a longer duration of VTS than applied in this study may induce a longer-lasting effect. For example, a 30-min muscle tendon vibration of wrist flexors induced an increase in corticospinal excitability of the antagonistic wrist extensors lasting for up to 60 min after vibration [41,42]. This result indicates that VTS can induce measurable and lasting changes in short-term cortical plasticity that exceeded those observed in this study. Moreover, a recent compendium study examining participants of the current sample who presented with neck pain [43], indicated that the effect of VTS on perceived pain tended to persist longer than the effect on head posture. At the 20-min retention timepoint the level of pain was still significantly lower when compared to baseline. It is noteworthy that participant demographics, disease severity and clinical manifestation did not predict the effects of VTS on CD symptoms.

4.2. Multiple VTS stimulation muscle sites may improve head posture

Prior to this study, there was no knowledge of what muscle sites or stimulation conditions (e.g., unilateral vs. bilateral, single vs. dual muscle) would be most effective for applying VTS. Given the various CD phenotypes with their involvement of different dystonic muscles, it seemed unlikely that a single condition was equally beneficial for all manifestations of CD. Thus, this study systematically evaluated possible VTS effects. The results indicated that several VTS stimulation conditions could be similarly effective in reducing an abnormal head posture. VTS of dystonic agonist muscles or their antagonists tended to yield the greatest change in HAI. For example, for participants with left torticollis, where the right SCM is usually involved, we found the greatest change in HAI for VTS of either right SCM and right SCM plus right TRP (contralateral rotators). For participants with right laterocollis, left and/or right SCM stimulation yielded the highest benefits (see Fig. 5B).

However, between-subject variability was large that even for an individual CD phenotype, the responsiveness to VTS did not solely depend on a specific muscle and did not necessarily have to involve the stimulation of the clinically identified dystonic muscles. These results are in line with earlier work on the effectiveness of a sensory trick in reducing EMG activity in dystonic muscles that demonstrated that sensory trick manoeuvres ipsi- or contralateral to the dystonic head rotation can be effective [44]. There are several possible explanations for this finding: First, given that many people with CD present with complex dystonic patterns involving more than one head rotational axis [32], the stimulation of muscle groups controlling movements around each axis can lead to a head righting effect. For example, stimulating both SCM and TRP may induce righting around the pitch and yaw axes (i.e., head extension and rotation). Second, the representations of body and muscle systems in the somatosensory and motor cortex are overlapping or "smeared" in patients with focal dystonia [13,16–18], which could explain why the stimulation of neighbouring muscles may yield a similar effect. In addition, research on inducing a tonic vibration reflex (TVR) in people with idiopathic focal dystonia through vibration of a muscle belly or tendon [13,45,46], found that the TVR was normal, suggesting intact functioning of the spinal reflex circuit, yet the perception of arm movement during the TVR was abnormal suggesting a pathologically altered integration of proprioceptive signals at supraspinal levels. Finally, consider that the VTS-induced effects on pain were also unspecific with multiple sites of stimulation being effective in different CD phenotypes [43].

4.3. Study control and limitations

It is imperative to recognize the study limitations that impact data interpretation and generalizability. First, this study was not designed to be a randomized clinical trial. It did not include a sham condition and one cannot rule out a possible contribution of placebo effect. However, consider that 57 out of 67 participants (85 %) responded to cervical VTS, which is considerably larger than the 35 % average placebo response reported in the placebo-controlled trials [47]. Relatedly, 26 % of participants responded to only one condition and most participants showed one "optimal" condition. If the observed VTS effects were solely a non-specific placebo effect, then one would have expected to see an unspecific response across all conditions. Thus, it is highly unlikely that the observed effects are fully attributable as a placebo across our sample of CD participants.

Second, participants received VTS only once. At this point we do not know the longitudinal effects of prolonged VTS. However, a recent study from our group [48] investigated the repeated use of VTS in people with laryngeal dystonia and found that the voice symptoms of those, who responded to VTS, repeatedly and consistently improved over an 11-week period and that these improvements were in addition to the benefits received from a BoNT injection. Third, SCM and TRP as the two most often affected muscles for CD were stimulated in this study. However, mechanoreceptors of deeper laying muscles such as splenius capitis or scalenus were likely not stimulated given the limited vibration amplitude of the used vibratory motors. Thus, we cannot exclude the possibility that some of the participants who did not show a positive response to VTS, would respond to the stimulation of deeper neck muscles.

5. Conclusion

This study provides the first systematic evidence of how people with CD respond to neck muscle VTS. Applying VTS led to fast, acute changes in head posture. Responsiveness to VTS was widespread with 85 % of participants showing biomechanically measurable head righting response, which corresponded closely to the 80 % of participants reporting that they use sensory tricks to mitigate dystonic symptoms. Nearly 40 % of participants exhibited large changes in abnormal head posture. A compendium study examining the participants of the current

sample who presented with neck pain [43], indicated that cervical VTS can also reduce neck pain in CD. These two findings together document that VTS broadly modulates a complex subcortical-cortical network involved in processing proprioceptive and nociceptive afferent signals (for a review, see Ref. [49]). The data presented here constitute an initial step towards establishing cervical VTS as a non-invasive neuromodulation treatment method for CD and potentially for other forms of FD. VTS could serve as an adjuvant therapy to established interventions such as BoNT injections.

CRediT authorship contribution statement

Laura Avanzino: Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Jiapeng Xu:** Writing – review & editing, Writing – original draft, Software, Methodology, Investigation, Data curation, Conceptualization. **Davide Martino:** Writing – review & editing, Writing – original draft, Conceptualization. **Antonella Conte:** Writing – review & editing, Writing – original draft, Conceptualization. **Stephanie Standal:** Investigation, Formal analysis. **Parisa Salehi:** Investigation, Formal analysis. **Sara Terranova:** Investigation, Formal analysis. **Gaia Bonassi:** Investigation, Formal analysis. **Parisa Alizadeh:** Investigation, Formal analysis. **Janet Adesewa Adeoti:** Investigation, Formal analysis. **Daniele Belvisi:** Investigation, Formal analysis. **Matteo Costanzo:** Investigation, Formal analysis. **Jinseok Oh:** Investigation, Formal analysis. **Jürgen Konczak:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Funding acquisition, Conceptualization.

Data availability

Data sets that do not contain personal identifiers and related health information can be made available upon reasonable request.

Funding

This research was partially supported by funds from the Translational Grant Program of the Office of Discovery and Translation at the University of Minnesota to JK.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We sincerely thank our group of participants for their time and effort, which made this study possible.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2025.107263.

References

[1] A. Albanese, K. Bhatia, S.B. Bressman, M.R. Delong, S. Fahn, V.S. Fung, et al., Phenomenology and classification of dystonia: a consensus update, Mov. Disord. 28 (7) (2013) 863–873.
[2] A. Macerollo, V. Sajin, M. Bonello, D. Barghava, S.H. Alusi, P.R. Eldridge, et al., Deep brain stimulation in dystonia: State of art and future directions, J. Neurosci. Methods 340 (2020) 108750.
[3] L. Marsili, M. Bologna, J. Jankovic, C. Colosimo, Long-term efficacy and safety of botulinum toxin treatment for cervical dystonia: a critical reappraisal, Expet Opin. Drug Saf. 20 (6) (2021) 695–705.
[4] M.C. Ridding, G. Sheean, J.C. Rothwell, R. Inzelberg, T. Kujirai, Changes in the balance between motor cortical excitation and inhibition in focal, task specific dystonia, J. Neurol. Neurosurg. Psychiatry 59 (5) (1995) 493–498.
[5] S. Rona, A. Berardelli, L. Vacca, M. Inghilleri, M. Manfredi, Alterations of motor cortical inhibition in patients with dystonia, Mov. Disord. 13 (1) (1998) 118–124.
[6] E. Tolosa, L. Montserrat, A. Bayes, Blink reflex studies in focal dystonias: enhanced excitability of brainstem interneurons in cranial dystonia and spasmodic torticollis, Mov. Disord. 3 (1) (1988) 61–69.
[7] A. Berardelli, J.C. Rothwell, M. Hallett, P.D. Thompson, M. Manfredi, C. D. Marsden, The pathophysiology of primary dystonia, Brain 121 (Pt 7) (1998) 1195–1212.
[8] A. Quartarone, M.F. Ghilardi, Neuroplasticity in dystonia: motor symptoms and beyond, Handb. Clin. Neurol. (2022) 207–218.
[9] A. Quartarone, D. Ruge, How many types of dystonia? Pathophysiological considerations, Front. Neurol. 9 (2018) 12.
[10] X. Huang, M. Zhang, B. Li, H. Shang, J. Yang, Structural and functional brain abnormalities in idiopathic cervical dystonia: a multimodal meta-analysis, Parkinsonism Relat. Disorders 103 (2022) 153–165.
[11] A. Conte, G. Defazio, M. Hallett, G. Fabbrini, A. Berardelli, The role of sensory information in the pathophysiology of focal dystonias, Nat. Rev. Neurol. 15 (4) (2019) 224–233.
[12] L. Avanzino, A. Cherif, O. Crisafulli, F. Carbone, J. Zenzeri, P. Morasso, et al., Tactile and proprioceptive dysfunction differentiates cervical dystonia with and without tremor, Neurology 94 (6) (2020) e639–e650.
[13] R.A. Grünewald, Y. Yoneda, J.M. Shipman, H.J. Sagar, Idiopathic focal dystonia: a disorder of muscle spindle afferent processing? Brain 120 (Pt 12) (1997) 2179–2185.
[14] J. Konczak, J.E. Aman, Y.W. Chen, K.Y. Li, P.J. Watson, Impaired limb proprioception in adults with spasmodic dysphonia, J. Voice 29 (6) (2015) 777, e17-23.
[15] N. Putzki, P. Stude, J. Konczak, K. Graf, H.C. Diener, M. Maschke, Kinesthesia is impaired in focal dystonia, Mov. Disord. 21 (6) (2006) 754–760.
[16] W. Bara-Jimenez, M.J. Catalan, M. Hallett, C. Gerloff, Abnormal somatosensory homunculus in dystonia of the hand, Ann. Neurol. 44 (5) (1998) 828–831.
[17] S. Butterworth, S. Francis, E. Kelly, F. McGlone, R. Bowtell, G.V. Sawle, Abnormal cortical sensory activation in dystonia: an fMRI study, Mov. Disord. 18 (6) (2003) 673–682.
[18] S. Meunier, L. Garnero, A. Ducorps, L. Mazieres, S. Lehericy, ST du Montcel, et al., Human brain mapping in dystonia reveals both endophenotypic traits and adaptive reorganization, Ann. Neurol. 50 (4) (2001) 521–527.
[19] S. Khosravani, J. Buchanan, M.D. Johnson, J. Konczak, Effect of neck botulinum neurotoxin injection on proprioception and somatosensory-motor cortical processing in cervical dystonia, Neurorehabilitation Neural Repair 34 (4) (2020) 309–320.
[20] R. Bianconi, MJ van der, The response to vibration of the end organs of mammalian muscle spindles, J. Neurophysiol. 26 (1963) 177–190.
[21] M.C. Brown, I. Enberg, P.B. Matthews, The use of vibration as a selective repetitive stimulus for Ia afferent fibres, J. Physiol. 191 (1) (1967) 31P, 2P.
[22] M.C. Brown, I. Engberg, P.B. Matthews, The relative sensitivity to vibration of muscle receptors of the cat, J. Physiol. 192 (3) (1967) 773–800.
[23] G.M. Goodwin, D.I. McCloskey, P.B. Matthews, Proprioceptive illusions induced by muscle vibration: contribution by muscle spindles to perception? Science 175 (4028) (1972) 1382–1384.
[24] G.M. Goodwin, D.I. McCloskey, P.B. Matthews, The contribution of muscle afferents to kinaesthesia shown by vibration induced illusions of movement and by the effects of paralysing joint afferents, Brain 95 (4) (1972) 705–748.
[25] J.P. Roll, J.P. Vedel, Kinaesthetic role of muscle afferents in man, studied by tendon vibration and microneurography, Exp. Brain Res. 47 (2) (1982) 177–190.
[26] R.J. Feiwell, K.J. Black, L.A. McGee-Minnich, A.Z. Snyder, A.M. MacLeod, J. S. Perlmutter, Diminished regional cerebral blood flow response to vibration in patients with blepharospasm, Neurology 52 (2) (1999) 291–297.
[27] L.W. Tempel, J.S. Perlmutter, Abnormal vibration-induced cerebral blood flow responses in idiopathic dystonia, Brain 113 (Pt 3) (1990) 691–707.
[28] S. Khosravani, A. Mahnan, I.L. Yeh, J.E. Aman, P.J. Watson, Y. Zhang, et al., Laryngeal vibration as a non-invasive neuromodulation therapy for spasmodic dysphonia, Sci. Rep. 9 (1) (2019) 17955.
[29] J.K. Tang, N. Mahant, D. Cunic, R. Chen, E. Moro, A.E. Lang, et al., Changes in cortical and pallidal oscillatory activity during the execution of a sensory trick in patients with cervical dystonia, Exp. Neurol. 204 (2) (2007) 845–848.
[30] A. Sedov, P. Joshi, U. Semenova, S. Usova, S. Asriyants, A. Gamaleya, et al., Proprioceptive modulation of pallidal physiology in cervical dystonia, Mov. Disord. 38 (11) (2023) 2094–2102.
[31] H.O. Karnath, J. Konczak, J. Dichgans, Effect of prolonged neck muscle vibration on lateral head tilt in severe spasmodic torticollis, J. Neurol. Neurosurg. Psychiatry 69 (5) (2000) 658–660.
[32] J. Jankovic, S. Leder, D. Warner, K. Schwartz, Cervical dystonia: clinical findings and associated movement disorders, Neurology 41 (7) (1991) 1088–1091.
[33] P. Cordo, V.S. Gurfinkel, L. Bevan, G.K. Kerr, Proprioceptive consequences of tendon vibration during movement, J. Neurophysiol. 74 (4) (1995) 1675–1688.
[34] P.J. Cordo, V.S. Gurfinkel, S. Brumagne, C. Flores-Vieira, Effect of slow, small movement on the vibration-evoked kinesthetic illusion, Exp. Brain Res. 167 (3) (2005) 324–334.
[35] A.G. Shaikh, D.S. Zee, H.A. Jinnah, Oscillatory head movements in cervical dystonia: dystonia, tremor, or both? Mov. Disord. 30 (6) (2015) 834–842.
[36] C. Boccagni, J. Carpaneto, S. Micera, S. Bagnato, G. Galardi, Motion analysis in cervical dystonia, Neurol. Sci. 29 (6) (2008) 375–381.

[37] J.P. Vu, E. Cisneros, J. Zhao, H.Y. Lee, J. Jankovic, S.A. Factor, et al., From null to midline: changes in head posture do not predictably change head tremor in cervical dystonia, Dystonia 1 (2022).
[38] C. Niewiadomski, R.J. Bianco, S. Afquir, M. Evin, P.J. Arnoux, Experimental assessment of cervical ranges of motion and compensatory strategies, Chiropr. Man. Ther. 27 (2019) 9.
[39] A.A.A. Sukari, S. Singh, M.H. Bohari, Z. Idris, A.R.I. Ghani, J.M. Abdullah, Examining the range of motion of the cervical spine: utilising different bedside instruments, Malays. J. Med. Sci. 28 (2) (2021) 100–105.
[40] Y. Benjamini, Y. Hochberg, Controlling the false discovery rate: a practical and powerful approach to multiple testing, J. Roy. Stat. Soc. B 57 (1) (1995) 289–300.
[41] A. Forner-Cordero, M. Steyvers, O. Levin, K. Alaerts, S.P. Swinnen, Changes in corticomotor excitability following prolonged muscle tendon vibration, Behav. Brain Res. 190 (1) (2008) 41–49.
[42] M. Steyvers, O. Levin, M. Van Baelen, S.P. Swinnen, Corticospinal excitability changes following prolonged muscle tendon vibration, Neuroreport 14 (15) (2003) 1901–1905.
[43] J. Xu, M. Costanzo, L. Avanzino, D. Martino, P. Salehi, S. Standal, et al., Vibro-tactile stimulation of the neck reduces pain in people with cervical dystonia: a proof-of-concept study, Neurol. Sci. 45 (10) (2024) 4847–4856.
[44] A. Schramm, K. Reiners, M. Naumann, Complex mechanisms of sensory tricks in cervical dystonia, Mov. Disord. 19 (4) (2004) 452–458.
[45] R. Kaji, J.C. Rothwell, M. Katayama, T. Ikeda, T. Kubori, N. Kohara, et al., Tonic vibration reflex and muscle afferent block in writer's cramp, Ann. Neurol. 38 (2) (1995) 155–162.
[46] Y. Yoneda, S. Rome, H.J. Sagar, R.A. Grunewald, Abnormal perception of the tonic vibration reflex in idiopathic focal dystonia, Eur. J. Neurol. 7 (5) (2000) 529–533.
[47] P. Enck, S. Klosterhalfen, K. Weimer, B. Horing, S. Zipfel, The placebo response in clinical trials: more questions than answers, Philos. Trans. R. Soc. Lond. B Biol. Sci. 366 (1572) (2011) 1889–1895.
[48] J. Konczak, D. Bhaskaran, N. Elangovan, J. Oh, G.S. Goding, P.J. Watson, Effects of an 11-week vibro-tactile stimulation treatment on voice symptoms in laryngeal dystonia, Front. Neurol. 15 (2024) 1403050.
[49] L. Avanzino, M. Tinazzi, S. Ionta, M. Fiorio, Sensory-motor integration in focal dystonia, Neuropsychologia 79 (Pt B) (2015) 288–300.